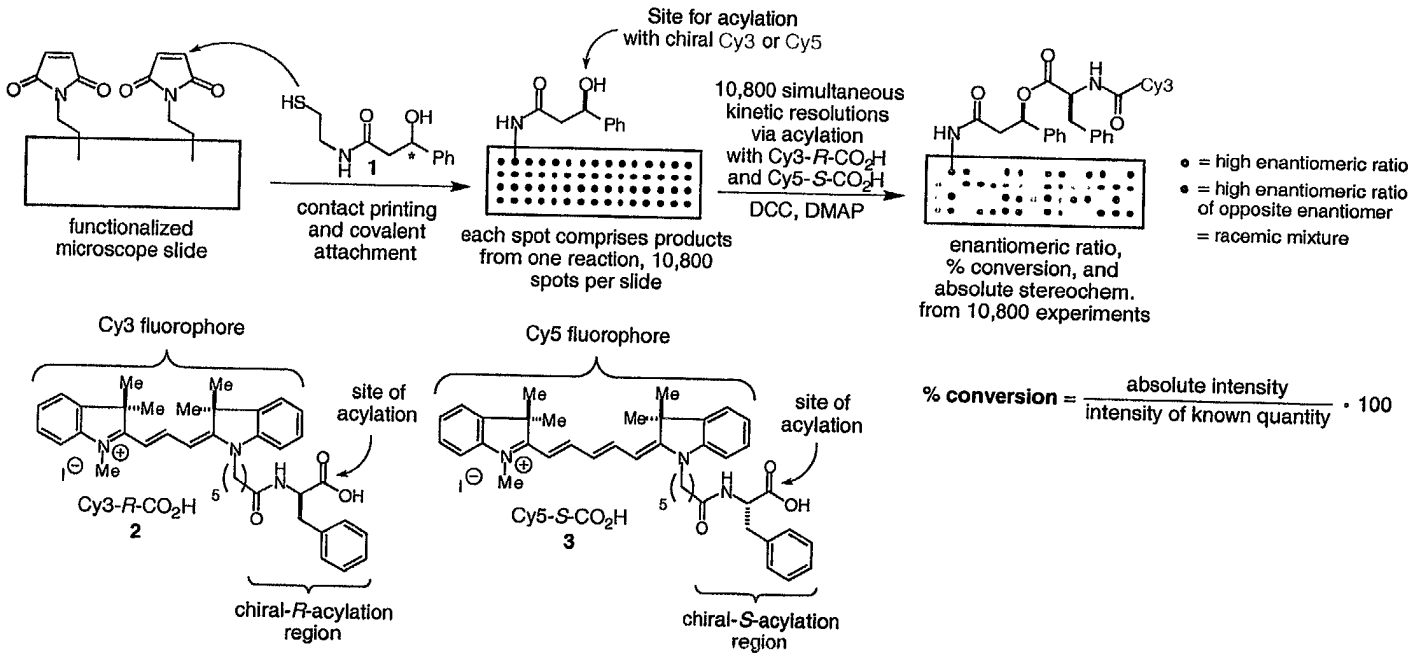

Site for acylation with chiral Cy3 or Cy5
functionalized microscope slide
contact printing and covalent attachment
each spot comprises products from one reaction, 10,800 spots per slide
10,800 simultaneous kinetic resolutions via acylation with Cy3-R-CO2H and Cy5-S-CO2H
DCC, DMAP
enantiomeric ratio, % conversion, and absolute stereochem. from 10,800 experiments
= high enantiomeric ratio
= high enantiomeric ratio of opposite enantiomer
= racemic mixture
Cy3 fluorophore
Cy3-R-CO2H
2
site of acylation
chiral-R-acylation region
Cy5 fluorophore
Cy5-S-CO2H
3
site of acylation
chiral-S-acylation region
% conversion = absolute intensity / intensity of known quantity · 100

Figure 1

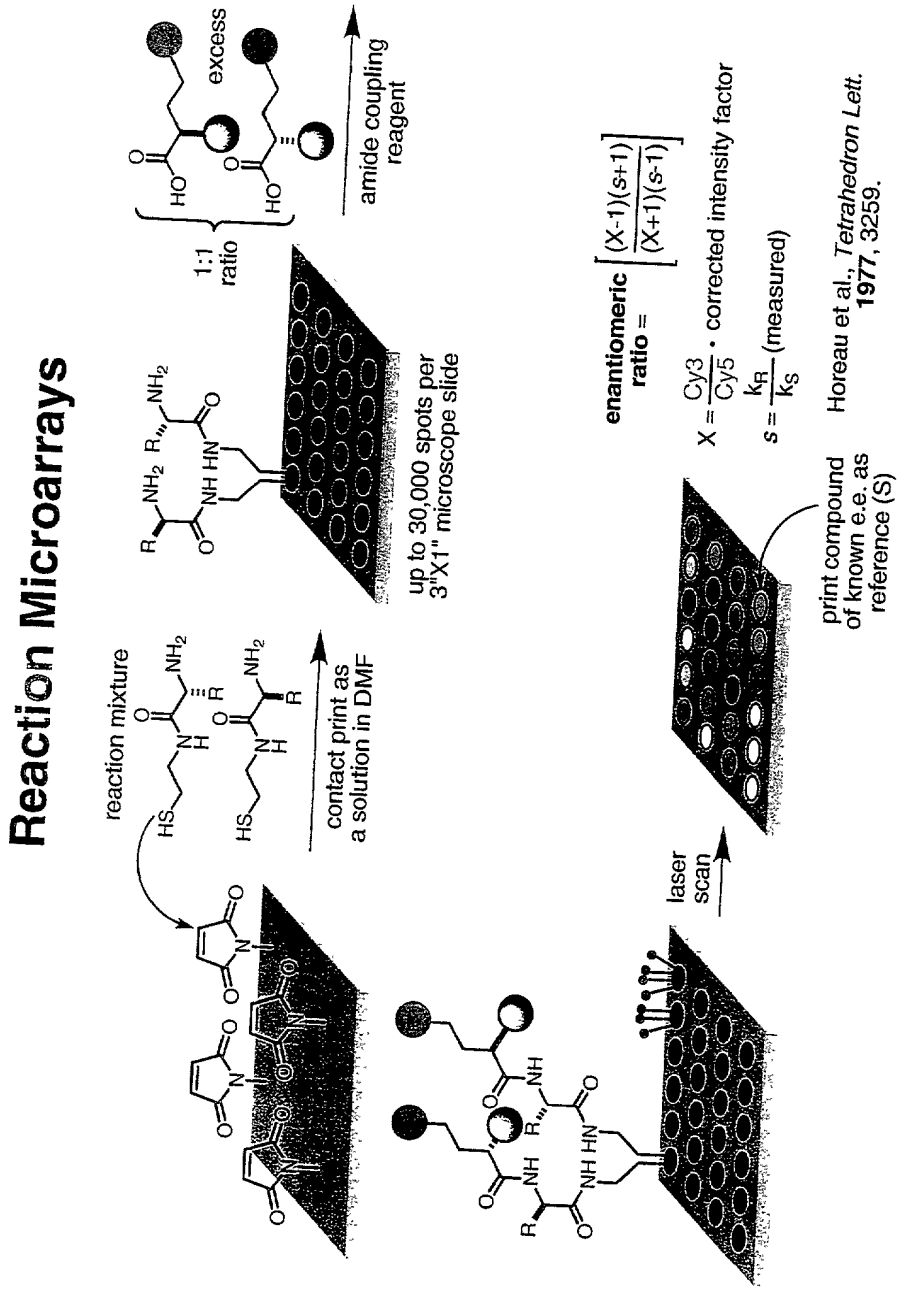

Reaction Microarrays
reaction mixture
contact print as a solution in DMF
up to 30,000 spots per 3"X1" microscope slide
1:1 ratio
excess
amide coupling reagent
laser scan
print compound of known e.e. as reference (S)
enantiomeric ratio = [(X-1)(s+1)/(X+1)(s-1)]
X = Cy3/Cy5 • corrected intensity factor
s = k_R/k_S (measured)
Horeau et al., Tetrahedron Lett. 1977, 3259.

Figure 2

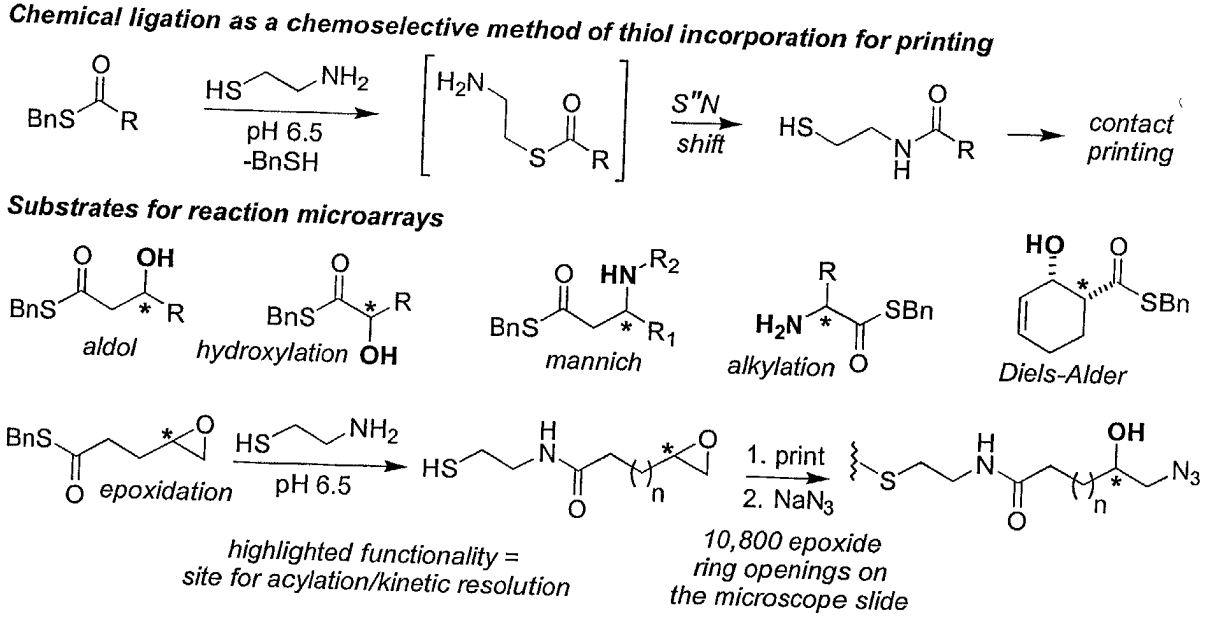
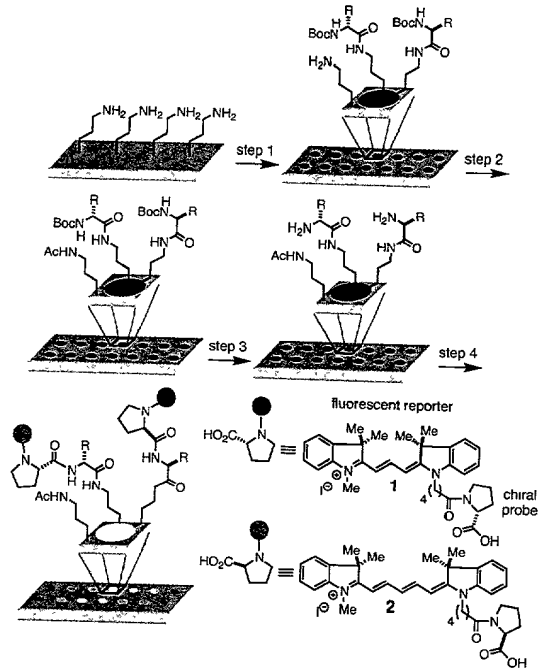

Chemical ligation as a chemoselective method of thiol incorporation for printing
BnS
R
HS
NH2
pH 6.5
-BnSH
H2N
S"N
shift
HS
N
H
contact
printing
Substrates for reaction microarrays
OH
aldol
hydroxylation
OH
HN
R2
R1
mannich
H2N
SBn
alkylation
HO
Diels-Alder
epoxidation
pH 6.5
1. print
2. NaN3
N3
highlighted functionality =
site for acylation/kinetic resolution
10,800 epoxide
ring openings on
the microscope slide

Figure 3



Reagents and conditions: step 1) BocHNCH(R)CO_2H, PyAOP, $^iPr_2NEt$, DMF, step 2) Ac_2O, pyridine; step 3) 10% CF_3CO_2H and 10% Et_3SiH in CH_2Cl_2, then 3% Et_3N in CH_2Cl_2; step 4) Pentafluorophenyl diphenylphosphinate, $^iPr_2NEt$, 1:1 mixture of **1** and **2**, DMF, -20 °C.

Figure 4

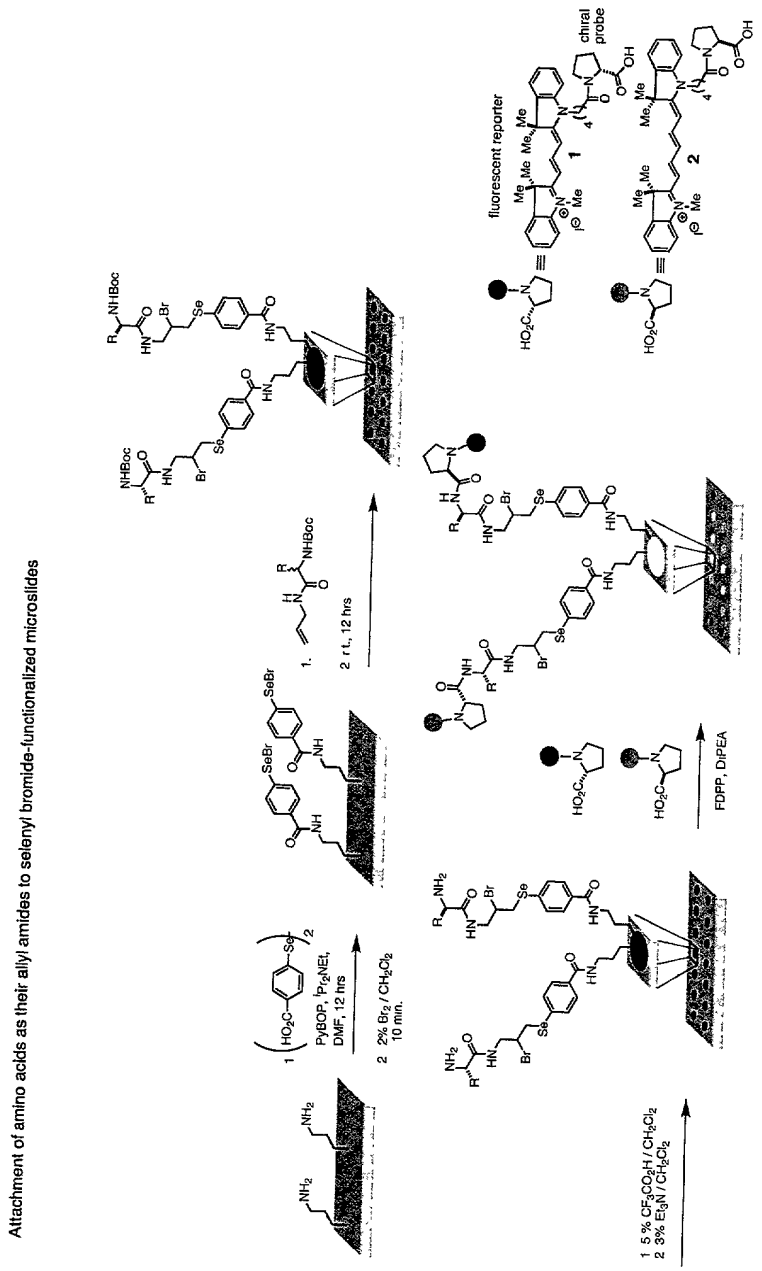

Attachment of amino acids as their allyl amides to selenyl bromide-functionalized microslides
1 (HO2C)
Se
2
PyBOP, iPr2NEt,
DMF, 12 hrs
2 2% Br2 / CH2Cl2
10 min.
SeBr
SeBr
1.
2 r.t., 12 hrs
NHBoc
1 5% CF3CO2H / CH2Cl2
2 3% Et3N / CH2Cl2
FDPP, DiPEA
fluorescent reporter
chiral
probe
1
2

Figure 5

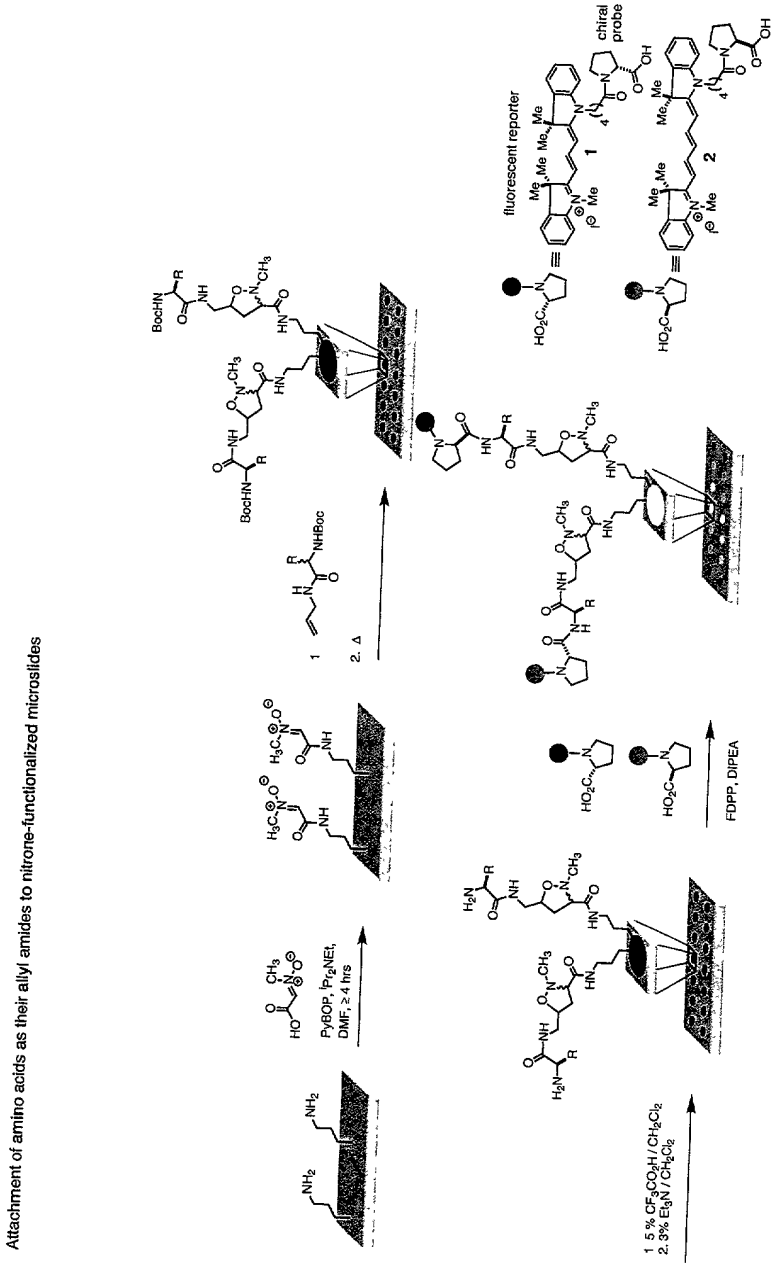

Attachment of amino acids as their allyl amides to nitrone-functionalized microslides
PyBOP, iPr2NEt, DMF, ≥ 4 hrs
1. Δ
2. Δ
fluorescent reporter
chiral probe
1
2
FDPP, DIPEA
1. 5% CF3CO2H / CH2Cl2
2. 3% Et3N / CH2Cl2

Figure 6

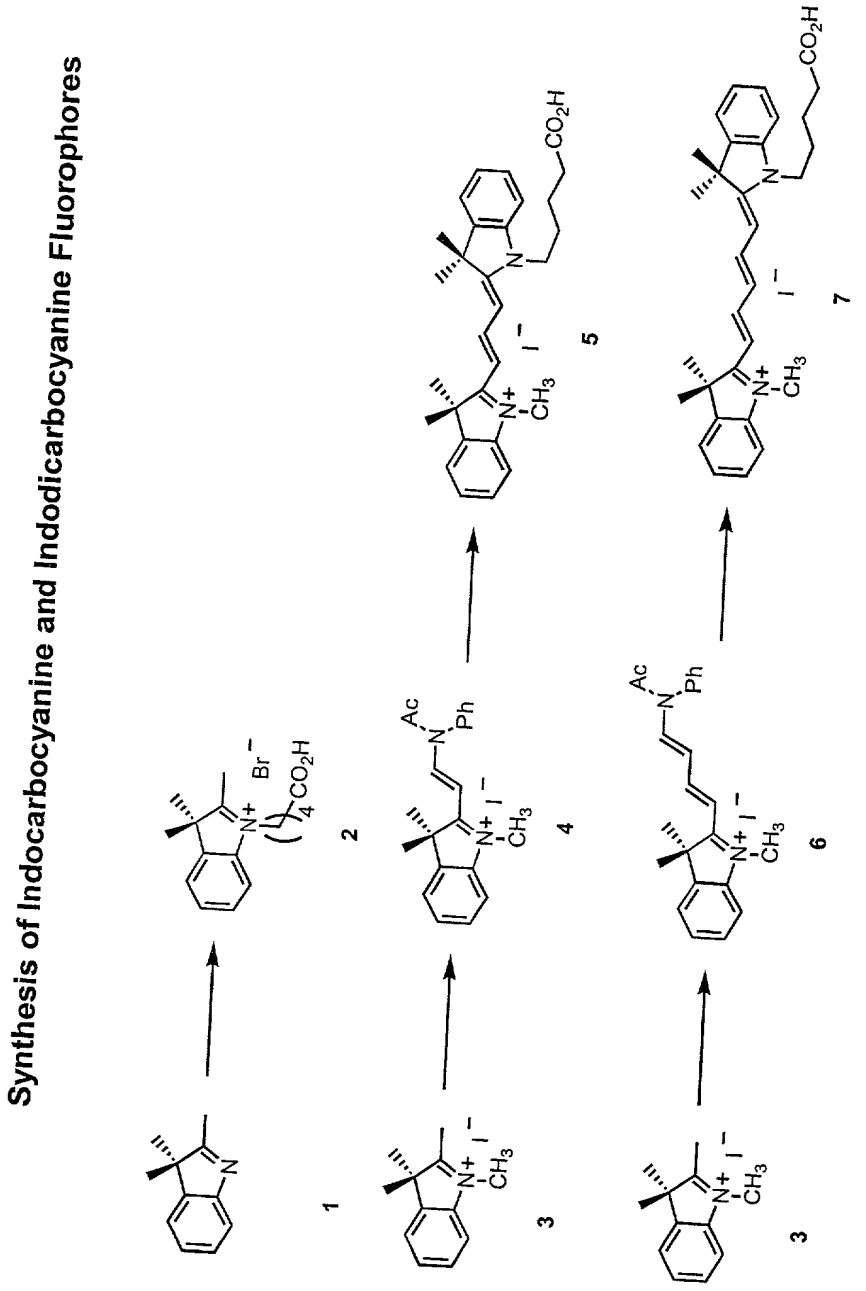

Synthesis of Indocarbocyanine and Indodicarbocyanine Fluorophores
1
2
3
4
5
6
7
3

Figure 7

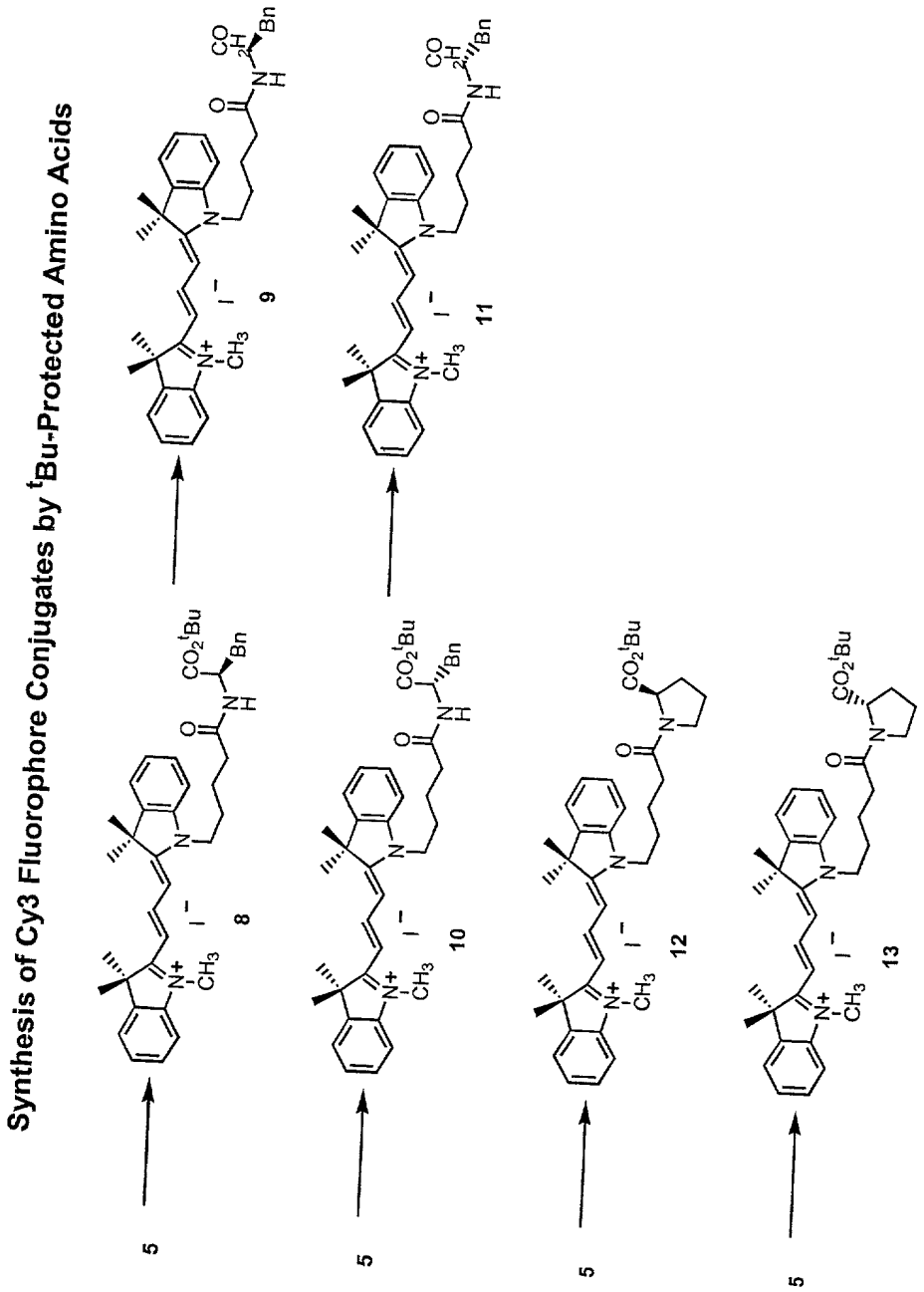

Synthesis of Cy3 Fluorophore Conjugates by tBu-Protected Amino Acids
5
8
9
10
11
12
13

Figure 8

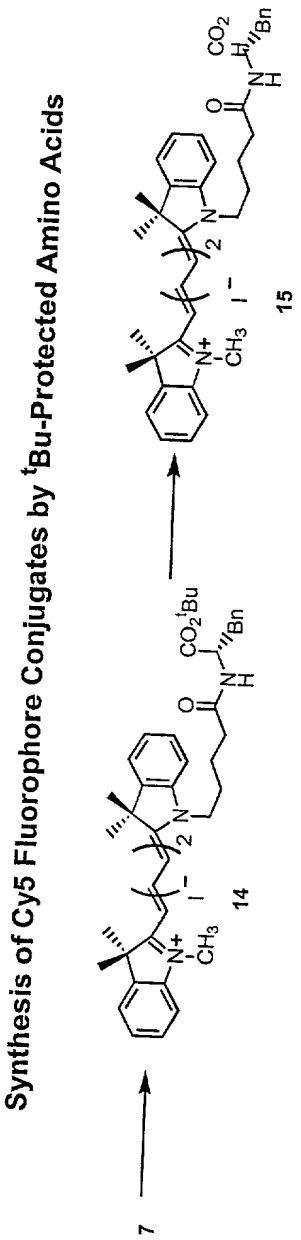
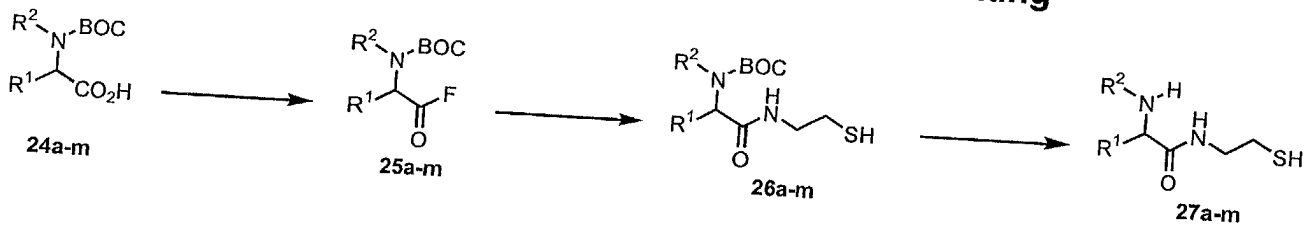

Synthesis of Cy5 Fluorophore Conjugates by tBu-Protected Amino Acids
7
14
15

Figure 9

Synthesis of Amino Acid Substrates for Printing



a $R^1 = R^2 = H$
(R)-b $R^1 = Me$, $R^2 = H$
(S)-c $R^1 = Me$, $R^2 = H$
(R)-d $R^1 = CH_2CH_2$-, $R^2 = CH_2$-
(S)-e $R^1 = CH_2CH_2$-, $R^2 = CH_2$-
(R)-f $R^1 = {}^iPr$, $R^2 = H$
(S)-g $R^1 = {}^iPr$, $R^2 = H$
(R)-h $R^1 = {}^tBu$, $R^2 = H$
(S)-i $R^1 = {}^tBu$, $R^2 = H$
(R)-j $R^1 = Ph$, $R^2 = H$
(S)-k $R^1 = Ph$, $R^2 = H$
(R)-l $R^1 = Bn$, $R^2 = H$
(S)-m $R^1 = Bn$, $R^2 = H$

Figure 10

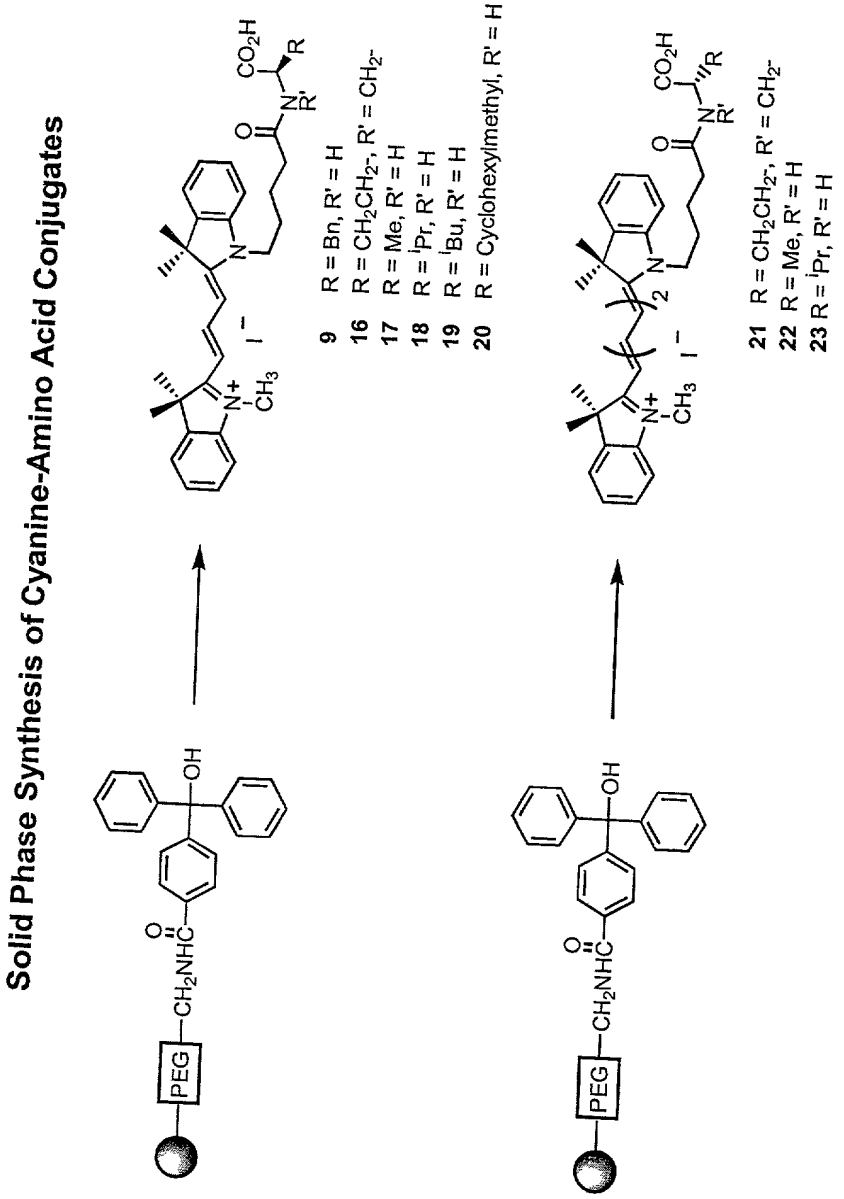
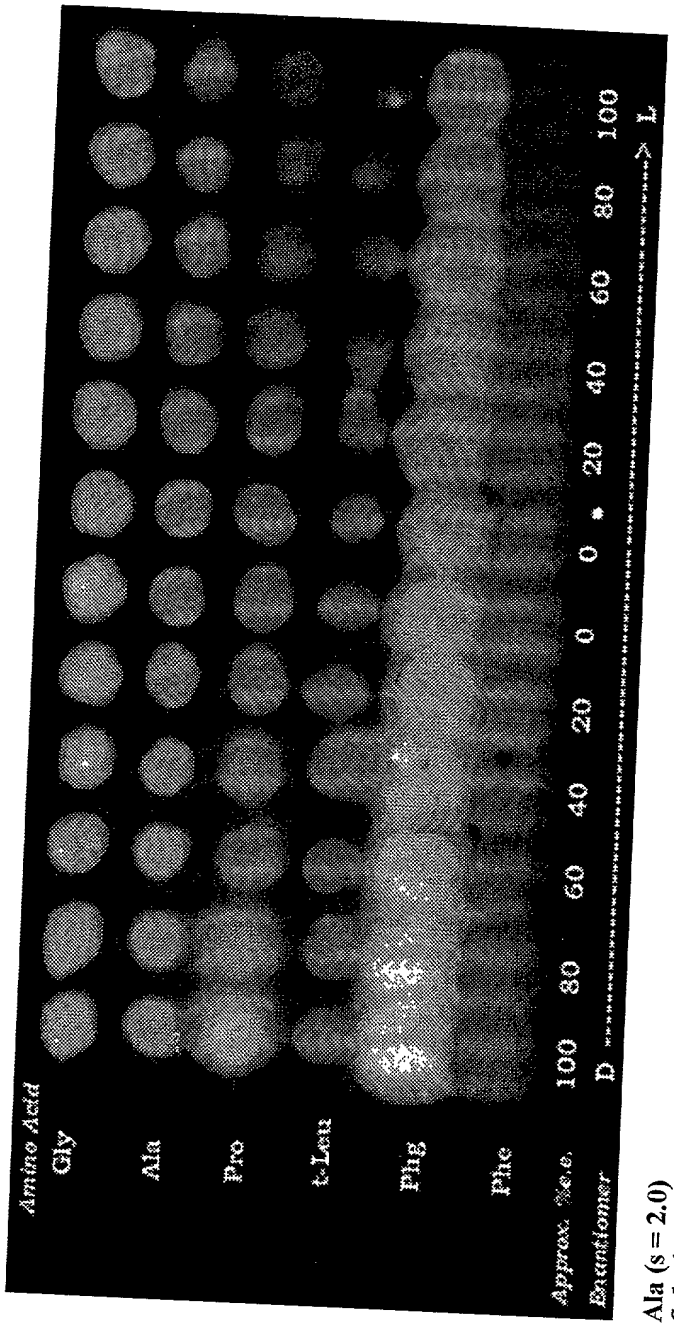
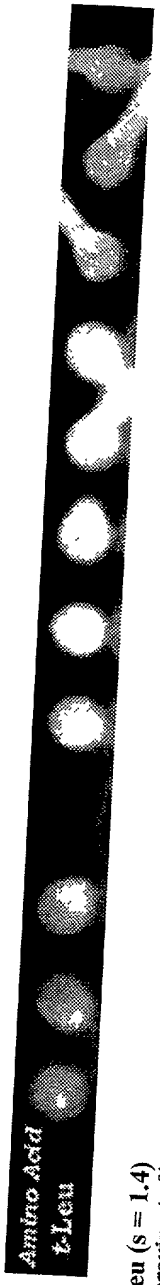

Solid Phase Synthesis of Cyanine-Amino Acid Conjugates
PEG
CH2NHC
OH
CO2H
CH3
I−
9 R = Bn, R' = H
16 R = CH2CH2-, R' = CH2-
17 R = Me, R' = H
18 R = iPr, R' = H
19 R = iBu, R' = H
20 R = Cyclohexylmethyl, R' = H
21 R = CH2CH2-, R' = CH2-
22 R = Me, R' = H
23 R = iPr, R' = H

Figure 11



Ala (s = 2.0)																		
Calculated %e.e	100	87.5	60.4	39.7	21.5	7.4	13.4	5.2	25.1	49.3	71.0	100						
Enantiomer	*D*	*D*	*D*	*D*	*D*	*D*	*D*	*L*	*L*	*L*	*L*	*L*						
Pro (s = 4.7)																		
Calculated %e.e	100	87.0	72.2	58.3	43.4	31.0	34.2	20.1	6.3	12.0	39.0	100						
Enantiomer	*D*	*D*	*D*	*D*	*D*	*D*	*D*	*D*	*D*	*L*	*L*	*L*						
Phe (s = 1.8)																		
Calculated %e.e	100	85.0	61.5	39.6	18.4	0.7	10.4	3.4	30.6	53.3	81.9	100						
Enantiomer	*D*	*D*	*D*	*D*	*D*	*D*	*D*	*L*	*L*	*L*	*L*	*L*						

Figure 12



t-Leu (s = 1.4)													
Approximate %e.e	100	80	60	40	20	0	20	40	60	80	100		
Calculated %e.e	100	55.3	28.8	N/A	33.7	34.8	37.6	6.8	6.3	46.0	70.8	100	
Expected enantiomer	D	D	D	D	D			L	L	L	L	L	
Enantiomer	D	D	D	N/A	D	D	D	D	L	L	L	L	

Figure 13

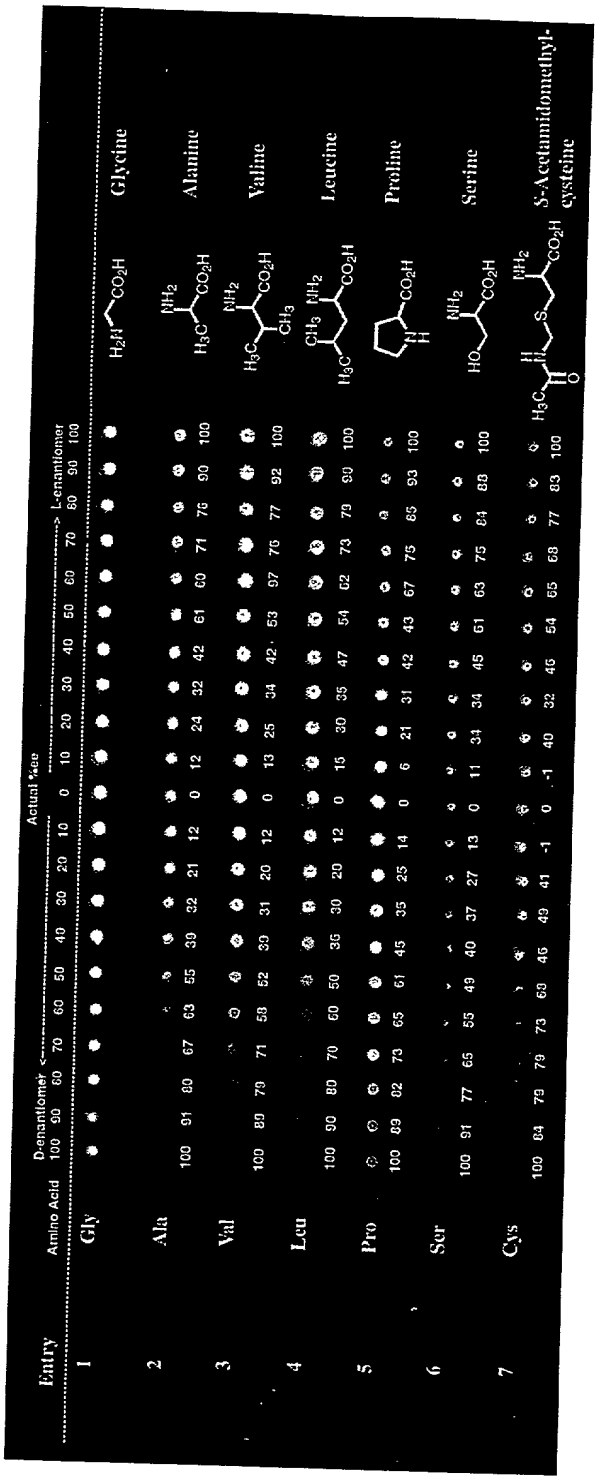

Entry
Amino Acid
D-enantiomer
Actual %ee
L-enantiomer
1 Gly
2 Ala
3 Val
4 Leu
5 Pro
6 Ser
7 Cys
Glycine
Alanine
Valine
Leucine
Proline
Serine
S-Acetamidomethyl-cysteine

Figure 14

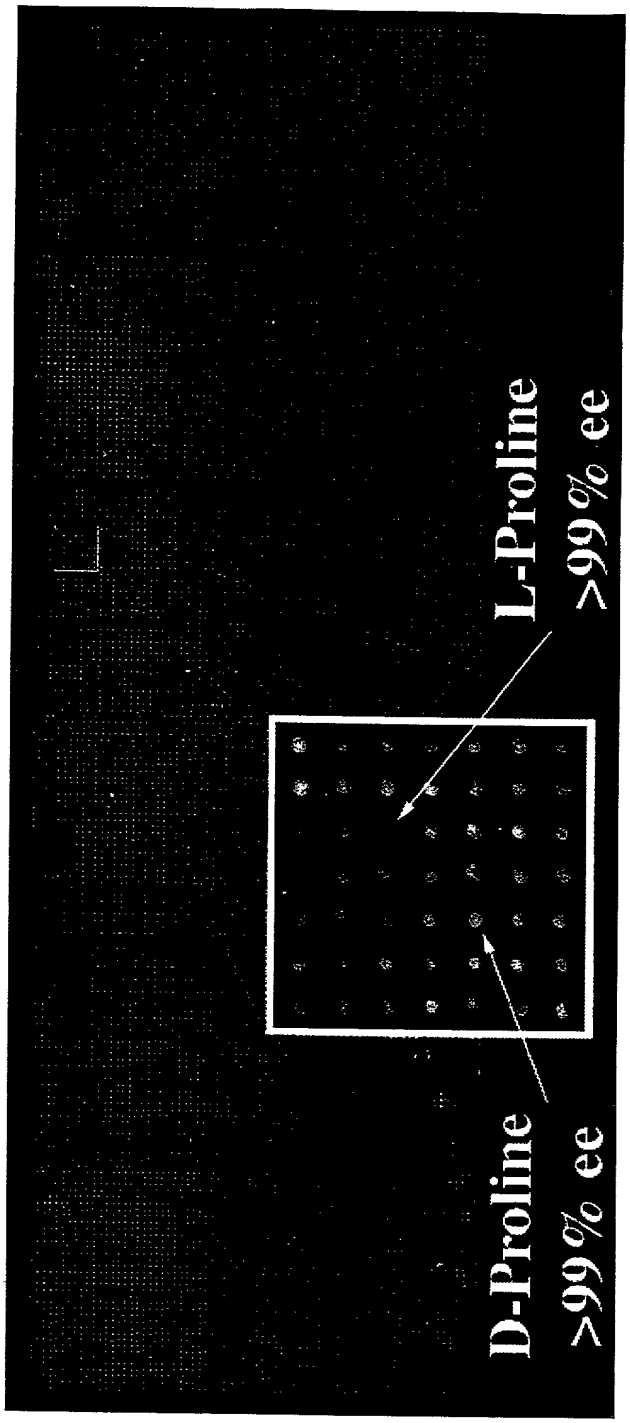


Figure 15